REMARKS/ARGUMENTS

Claims 3-6 and 12-17 have been withdrawn as the result of an earlier restriction requirement without prejudice to Applicant's right to pursue the subject matter of the withdrawn claims in one or more related applications.

Applicant acknowledges the Examiner's reconsideration of the restriction requirement and the examination of Groups I and II, species Groups A-L and thanks the Examiner for her consideration of Applicant's arguments and examination of the claims.

No new matter has been introduced as a result of amendments to the specification and the claims.

Amendments to the Specification

Paragraph 0049 has been amended to include reference to SEQ ID NO. 33. Typographical errors have been corrected in paragraphs 0049, 0053 and 0054.

Claim Objections

Claims 18 and 19 were objected to because of informalities. Claims 18 and 19 have been amended to incorporate the elements of withdrawn claim 14 and new claims 27 and 28 incorporate the elements of withdrawn claim 17.

Claims 21 and 22 have been amended to correct an error in dependency. The amended claims now correctly depend from claim 20.

Claim Rejections under 35 U.S.C. §112

Claim 24 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 has been amended to include reference to SEQ ID NO. 33. Furthermore, a substitute sequence listing is submitted herewith to include SEQ ID NO. 33.

Claim Rejections under 35 U.S.C. §102

Claim 20 stands rejected under 35 U.S.C. §102(b) as being anticipated by Moyer *et al.* (US Patent No. 5,212,057). The Examiner states in the Office Action mailed April 14, 2006 on page 4, "Moyer *et al.* teaches a vaccine construct comprising any avirulent poxvirus modified by insertion of a marker gene from a different poxvirus (see column 4, lines 8-49). Moyer *et al.* teach recovery of recombinant viral progeny, which would comprise a complex of polypeptides comprising external immunogens of cross-reactive polypeptides." Applicant respectfully disagrees with the Examiner.

Moyer *et al.* discloses novel poxvirus vectors wherein the vector comprises any avirulent member of the poxvirus family as long as the poxvirus is capable of growth. Specifically, Moyer *et al.* discloses deletion mutants. Moyer *et al.* does not disclose a vector comprising external immunogen polyproteins of poxviruses. Furthermore, Moyer *et al.* discloses using the entire replication competent poxvirus in the construction of vectors. The present application discloses subunit vaccines which do not comprise the entire virus (paragraph 0030) and are non-replicating (paragraph 0038).

Applicant has amended claim 20 to incorporate the element "wherein said complex is not an entire virus." Support for this amendment can be found in the specification in paragraph 00030. Amended claim 20 is reproduced below:

> 20. An immunogenic composition comprising a complex of polypeptides wherein each polypeptide comprises an external immunogen of a membrane-associated protein of variola major or immunologically cross-reactive poxviruses and wherein said complex is not an entire virus.

A claim is anticipated under 35 U.S.C. §102(b) only if each and every element as set forth in a claim is found, either expressly or inherently described, in a single prior art reference (MPEP §2131; *Verdegaal Bros. V. Union Oil Co. of California*, 2 U.S.P.Q.2d 1051 (Fed. Cir. 1987)). Moyer *et al.* do not disclose "an immunogenic composition comprising a complex of polypeptides wherein each polypeptide comprises an external immunogen of a membrane-associated protein of variola major or immunologically cross-reactive poxviruses and wherein said complex is not an entire virus." Therefore

claim 20 of the instant application is not anticipated by Moyer *et al* and Applicant respectfully requests that the 35 U.S.C. §102(b) rejection of claim 20 over Moyer *et al.* be withdrawn.

Claim Rejections under 35 U.S.C. §103(a)

Claims 1-2, 7-11 and 18-20 stand rejected under 35 U.S.C. §103(a) as being unpatentable over US Patent Application No. 09/781,124 (Hooper *et al.*). and Thomson *et al.* (The Journal of Immunology, 1998, Vol. 160, pgs. 1717-1723). Claim 21 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Hooper *et al.* in view of Thomson *et al.* and Curiel *et al.* (US Patent No. 6,274,322). Claim 22 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Hooper *et al.* in view of Thomson *et al.* and Rutter *et al.* (US Patent Publication No. 2002/0015707 A1). Claims 23-26 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Hooper *et al.* in view of Thomson *et al.* and Newton *et al.* (Biochemistry, 1996, Vol. 35, pgs. 545-553).

Applicants respectfully submit that the Examiner has not established *prima facie* obviousness of claims 1-2, 7-11 and 18-26 and new claims 27 and 28 in view of the cited references, as these references, either alone or in combination, do not teach or suggest each and every element of the invention as presently claimed.

To reject a claim under 35 U.S.C. §103(a), the Examiner bears the initial burden of showing an invention to be *prima facie* obvious over the prior art. *In re Bell*, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1992). If the Examiner cannot establish a *prima facie* case of unpatentability, then without more the applicant is entitled to grant of the patent. *In re Oetiker*, 24 U.S.P.Q.2d 1443 (Fed Cir. 1992). The Examiner must meet a three-part test to render a claimed invention *prima facie* obvious.

To begin with, the prior art references cited by the Examiner must provide "motivation, suggestion, or teaching of the desirability of making the specific combination that was made by the application." *In re Kotzab*, 55 U.S.P.Q.2d 1316 (Fed. Cir. 2000). Where an obviousness determination relies on the combination of two or more references, there must be some suggestion or motivation to combine the references. *WMS Gaming Inc. v. International Game Technology*, 51 U.S.P.Q.2d 1386

(Fed. Cir. 1999). The suggestion may be found in implicit or explicit teachings within the references themselves, from the ordinary knowledge of one skilled in the art, or from the nature of the problems to be solved. *Id.*

Second, the prior art references cited by the Examiner must suggest to one of ordinary skill in the art that the invention would have a reasonable expectation of success. *In re Dow Chemical*, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). The expectation of success, like the motivation to combine two prior art references, must come from the prior art, not the applicant's disclosure. *Id.*

Finally, the Examiner must demonstrate that the prior art references, either alone or in combination, teach or suggest each and every limitation of the rejected claims. *In re Gartside*, 53 U.S.P.Q.2d 1769 (Fed. Cir. 2000).

If any one of these three factors is not met, the PTO has failed to establish *prima facie* obviousness and the applicant is entitled to grant of a patent without making any affirmative showing of non-obviousness.

Applicant will address each rejection individually.

Claims 1-2, 7-11, and 18-20 rejected under 35 U.S.C. §103(a) as unpatentable over Hooper et al. (hereinafter 'Hooper') and Thomson et al. (hereinafter 'Thomson')

Hooper discloses an immune globulin composition comprising one or more monoclonal antibodies against vaccinia antigens (paragraph 0005) wherein the monoclonal antibodies are neutralizing antibodies. Hooper further discloses that antibodies against the vaccinia gene products L1R and A33R are preferred antigens. Hooper does not teach nor suggest polyproteins or immunogenic compositions comprised of polyproteins.

Thomson discloses delivery of multiple epitope DNA vaccines for the induction of cytotoxic T lymphocyte (CTL) responses. Thomson discloses that the DNA vaccines comprise a series of minimal CTL epitopes and that the DNA encoding the epitopes comprises only the epitope sequence and not any other portion of the gene of interest (page 171, column 2, first paragraph continued from column 1). Thomson does not

teach or suggest polyproteins, which are defined in the instant application in paragraph 0027 as "more than one protein, or polypeptide, made as a result of a single transcription event that has not been cleaved into individual protein, or polypeptide chains."

The combination of Hooper and Thomson does not teach or suggest polyproteins, or immunogenic compositions comprised of polyproteins, all elements of claims 1-2, 7-11, 18-20 and new claims 27 and 28. Furthermore, combining the teachings of Hooper with the teachings of Thomson would not create the polyprotein of the instant application with a reasonable expectation of success. Hooper teaches neutralizing monoclonal antibodies to vaccinia while Thomson teaches polyepitope vaccines to induce CTL responses. It would be well known to a person of ordinary skill in the art that neutralizing antibodies are induced by surface or secreted antigens and CTL responses are induced by antigens which have been processed, degraded and associated with self class I MHC molecules. Therefore, a person or ordinary skill would not seek to combine methods for the generation of CTL responses with antigens for the generation of neutralizing antibodies. Moreover, based at least in part on the lack of a reasonable expectation of success, there is no motivation to combine Hooper with Thomson.

Based on the foregoing, Applicant respectfully submits that (i) Hooper and Thomson, either singly or in combination, do not teach or suggest each and every element of claims 1-2, 7-11, 18-20 and 27-28; (ii) there would be no reasonable expectation of success to generate the presently claimed invention based on the combination of Hooper and Thomson; and (iii) there is no motivation to combine these references. Therefore the Examiner has not established *prima facie* obviousness of claims 1-2, 7-11, 18-20 and 27-28 based on Hooper and Thomson.

Claim 21 rejected under 35 U.S.C. §103(a) as unpatentable over Hooper in view of Thomson and in further view of Curiel et al. (hereinafter 'Curiel')

Claim 21 has been amended to correct dependency and is now dependent on claim 20. It has been determined *supra* that claim 20 is not *prima facie* obvious over

Hooper in view of Thomson because these references do not teach or suggest each and every element of independent claim 20, there is not a reasonable expectation of success from combining these references and there is no resulting motivation to combine them.

The deficiencies of Hooper and Thomson as invalidating 35 U.S.C. §103(a) art are not remedied by Curiel. Curiel teaches viral conjugates wherein the virus and a nucleic acid binding domain are bound by a biotin-streptavidin bridge.

The combination of Hooper, Thomson and Curiel do not teach or suggest all the elements of claim 21, specifically immunogenic compositions comprised of complexes of polypeptides wherein each polypeptide comprises an external immunogen of a membrane-associated protein of variola major or immunologically cross-reactive poxviruses wherein the polypeptides are biotinylated and the complex is formed by the additional of avidin or streptavidin.

Therefore Applicant respectfully submits that the cited references, either singly or in combination, do not teach or suggest each and every element of claim 21 and therefore the Examiner has not established *prima facie* obviousness of claim 21 based on Hooper in view of Thomson and Curiel.

Claim 22 rejected under 35 U.S.C. §103(a) as unpatentable over Hooper in view of Thomson and in further view of Rutter et al. (hereinafter 'Rutter')

Claim 22 has been amended to correct dependency and is now dependent on claim 20. It has been determined *supra* that claim 20 is not *prima facie* obvious over Hooper in view of Thomson because these references do not teach or suggest each and every element of independent claim 20, there is not a reasonable expectation of success to generate the presently claimed invention based on the combination of these references, and, as a result, there is no motivation to combine them.

The deficiencies of Hooper and Thomson are not remedied by Rutter. Rutter discloses agents to facilitate the delivery of a viral subunit vaccine wherein the agent is a liposome.

The combination of Hooper, Thomson and Rutter does not teach or suggest all the elements of claim 22, specifically immunogenic compositions comprised of complexes of polypeptides wherein each polypeptide comprises an external immunogen of a membrane-associated protein of variola major or immunologically cross-reactive poxviruses when the complex is formed by anchoring the polypeptides in a liposome or micelle.

Therefore Applicants respectfully submit that the cited references, either singly or in combination, do not teach or suggest each and every element of claim 22 and therefore the Examiner has not and cannot establish *prima facie* obviousness of claim 22 based on Hooper in view of Thomson and Rutter.

Claims 23-26 rejected under 35 U.S.C. §103(a) as unpatentable over Hooper in view of Thomson and further in view of Newton et al. (hereinafter 'Newton').

Claims 23-26 are not *prima facie* obvious over Hooper in view of Thomson as discussed *supra* because these references do not teach or suggest each and every element of claims 23-26, there is not a reasonable expectation of success to generate the presently claimed invention based on the combination of these references, and, as a result and there is no motivation to combine them.

The deficiencies of Hooper and Thomson are not remedied by Newton. Newton discloses linkers to link peptides wherein the linkers include a $(GGGGS)_3$ linker. Newton also teaches affinity tags.

The combination of Hooper, Thomson and Newton does not teach or suggest all the elements of independent claim 23, specifically a polyprotein comprising external immunogens of membrane-associated proteins of variola major or immunologically cross-reactive poxviruses wherein the individual proteins are jointed through a linker-spacer peptide. Therefore Applicant respectfully submits that the cited references, either singly or in combination, do not teach or suggest each and every element of claims 23-26 and therefore the Examiner has not established *prima facie* obviousness of claims 23-26 over Hooper in view of Thomson and Newton.

In view of the foregoing, Applicant respectfully submits that none of Hooper, Thomson, Curiel, Rutter or Newton, either alone or in combination, teach or suggest polyproteins comprising external immunogens of membrane-associated proteins of variola major or immunologically cross-reactive poxviruses or immunogenic compositions comprising such polyproteins. Furthermore, there is no expectation of success nor motivation to combine Hooper and Thomson. Therefore Applicants respectfully submit that the Examiner cannot establish *prima facie* obviousness of claims 1-2, 7-11 and 18-28. Accordingly, Applicant respectfully submits that claims 1-2, 7-11 and 18-28 are not obvious under 35 USC §103(a) over the cited prior art and request the withdrawal of the outstanding rejections on this basis.

Conclusion

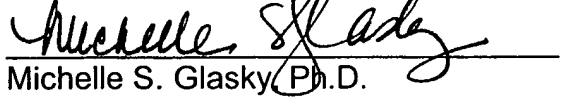
As a result of these Amendments and Remarks, claims 1-2, 7-11 and 18-28 are pending. Claims 18 and 19 have been canceled.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

The Commissioner is authorized to charge any fee which may be required in connection with this Amendment to deposit account No. 50-3207.

Respectfully submitted,

Dated: 7/14/06



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